REMARKS

Applicant's attorney appreciates the courteous interview extended the undersigned on January 16, 2007. During the interview, the objection to the claims under 35 U.S.C. § 112, the rejection of the claims under 35 U.S.C. § 103(a) and the finality of the present Office Action was discussed. The Examiner indicated that an allowance would be forthcoming in the present case if certain amendments were presented along with substantive comment on the record regarding the appropriateness of the amendments. The amendments discussed during the interview are presented herein for further consideration by the Examiner along with the following remarks. It is respectfully submitted that the claims presented herein are in condition for final allowance, and notice to such effect is respectfully requested.

Currently claims 1, 4-10, 11, 13, 15-16 and 19-23 are pending. Claims 3, 14 and 24-91 have been canceled and claims 2, 12 and 17-18 were previously withdrawn. Claims 1, 9-11, 19, 20-21 and 23 have been amended and claims 92 and 93 have been added.

Initially, it is respectfully submitted that finality of the Office action dated November 1, 2006 is premature. As was discussed during a telephone conference with the Examiner on December 28, 2006 and the interview of January 16, 2007, the finality of the present Office action is inappropriate because the new ground of rejection was not necessitated by Applicant's amendment, nor was it based on information submitted in an IDS. As the Examiner knows, a second action should not be made final if it includes a new rejection of a previously presented claim or a limitation which should reasonably have been expected to be claimed. (MPEP 706.07(a)). In the last response, Applicant amended claim 1 to recite a dsRNA (an element previously presented in original claim 14). The Examiner even acknowledged that the dsRNAs disclosed in the specification were adequately described in the specification. Accordingly, the subsequent response dated October 12, 2006, wherein Applicant amended the claims to specifically recite dsRNA, should have been expected, and the rejections in the current action could have been cited in the previous office action. Making this Office action "Final" deprives Applicant of an opportunity to address substantive aspects of the rejection. It is respectfully requested that the finality of the office action is premature, and respectfully requests that the finality of the action been withdrawn.

Priority

As requested by the Examiner, an English translation of provisional application No. 60/431,173 and a statement that the translation is accurate is submitted herewith.

Double Patenting

The Examiner has provisionally rejected claims 1, 3-11, 13, 15, 16 and 20-23 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5-13, 16, 21, 44 and 47 of copending U.S. Application No. 10/511,656. Applicant submits herewith a terminal disclaimer. Accordingly, this rejection is rendered moot.

Claim Objection

The Examiner has noted that claim 11 was incorrectly indicated as withdrawn. Applicant hereby correct the status identifier of claim 11 to recite that claim 11 is pending and is currently amended to recite the elected subject matter. Accordingly, this objection is moot. Claim 19 has been objected to because the claim recites both a nucleotide sequence and an amino acid sequence of SEQ ID No. 3, however SEQ ID NO. 3 is a DNA nucleic acid sequence. Applicant has amended claim 19 to clarify that the sequence comprises SEQ ID NO.3. Accordingly, this objection is moot.

35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 1, 3-10, 13 and 20-23 under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification to reasonably convey to one skilled in the art that the inventor(s) had possession of the claimed invention. As discussed during the interview, the claims have been amended to focus on a method of treating a disorder of the eye by administering outside of the blood-retina barrier a dsRNA compound of fifteen (15) to thirty (30) nucleotides in length, more preferably, twenty-one (21) to twenty-three (23) nucleotides in length (see claim 15). Support for such an amendment may be found at, for example, paragraph [0177] and the originally presented claims. There is no confusion over the metes and bounds of Applicant's claimed invention. The Applicant has provided specific structural and functional guidance for the dsRNA that enables one ordinarily skilled in the art to immediately envision the genus of compounds that may be administered outside the blood-retina barrier. Moreover, the Applicant has provided specific examples of methods of administering dsRNA outside the blood-retina barrier as evidenced by,

for example, Example 21 that describes the specific post transcriptional gene silencing by dsRNA of the target gene eGFP in the retinal pigment epithelium (RPE) and the retina of transgenic mice following systemic administration. As discussed and agreed upon during the interview, the Applicant has adequately described the method of treating a disorder of the eye by administering outside the blood-retina barrier a dsRNA of 15 to 30 nucleotides in length, has provided structural guidance as to the genus of compounds being covered, and provides *in vivo* data in support for the present claims. The Examiner agreed that the inclusion of the length of the dsRNA being between 15 to 30 nucleotides would serve to further define the dsRNA used in the claimed method an eliminates concerns expressed by the Examiner. Accordingly, Applicant requests that this rejection be withdrawn.

35 U.S.C. § 103

The Examiner rejected claims 1, 3-11, 13, 15, 16 and 19-23 under 35 U.S.C. § 103(a) as being unpatentable over Robinson, Dryja, Weber, Epstein, Elbashir and Bass. Specifically, the Examiner has asserted that Robinson purportedly discloses the administration of antisense oligonucleotides intraocularly to cells in the eyes to treat diseases associated with the eye, Dryja purportedly discloses that cGMP phosphodiesterase may be involved in various, specified ocular disorders and Epstein purportedly discloses that antisense oligonucleotides may regulate phosphodiesterase genes. Further, the Examiner asserts that Elbashir discloses that siRNAs may suppress the expression of genes in various mammalian cell lines, and the Elbashir and Bass purportedly disclose that siRNAs can be used to produce the same or potentially more robust effect as antisense oligonucleotides. Accordingly, the Examiner asserts that it would have been obvious to one ordinarily skilled in the art to use siRNAs as taught by Elbashir and Bass to inhibit the expression of a target gene, specifically the beta subunit of rod cGMP phosphodiesterase, and the development of ocular diseases associated with the expression of this target gene. Applicant respectfully disagrees.

As amended and discussed during the interview, the claims are directed to administering a therapeutically effective amount of a siRNA outside the blood-retina barrier to inhibit expression of a target gene to treat a disorder of the eye. None of the cited references alone or in combination teach the administration of an antisense oligonucleotide, let alone a dsRNA, outside the blood-retina barrier to modulate a target gene. The Examiner's primary reference, Robinson, in fact teaches away from the claimed invention by teaching administration

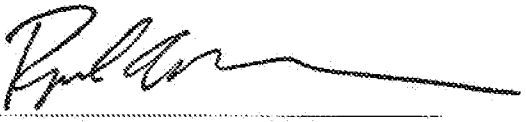
of antisense oligonucleotides by intravitreal injection (administration inside the blood-retina barrier). The other references do little more than describe inhibition of a target gene *in vitro*. There is no teaching that antisense oligonucleotides would be effective in inhibiting the expression of a target gene when administered outside the blood-retina barrier. In fact, the value of antisense technology relies heavily on delivery vehicles and mechanisms of delivery. At the time of the Applicant's present invention, one of ordinary skill in the art would not have been motivated to treat a disease of they eye by administering antisense, let alone dsRNA, outside the blood-retina barrier. As acknowledged by the Examiner, the Bass reference relied on by the Examiner discloses that even siRNA use *in vitro* (i.e., in mammalian cells) has been problematic (*see* Bass, page 428, Column 1). Accordingly, one ordinarily skilled in the art would not have had a reasonable expectation of success in administering dsRNA *in vivo*, and more specifically administration of dsRNA outside the blood-retina barrier. Applicant demonstrated that dsRNA may be administered outside the blood-retina barrier to effectively treat a disease of the eye. None of the cited references alone or in combination teach the use of dsRNA by administering dsRNA outside the blood-retina barrier to modulate a target gene, let alone provide one ordinarily skilled in the art with a reasonable expectation of success. Applicant requests that the rejection be withdrawn and the present claims allowed. Notice to such effect is respectfully requested.

CONCLUSION

Applicant have timely filed this response. In the event that a fee is required for this response, the Commissioner is hereby authorized to charge such fees to Deposit Account No. 50-0436.

Should the Examiner have any questions or comments, or need any additional information from Applicant's attorney, he is invited to contact the undersigned at his convenience.

Respectfully submitted,

By: 

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